Department of Pesticide Regulation

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Director

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M E M O R A N D U M

TO: Joseph P. Frank
Senior Toxicologist
Worker Health and Safety Branch

FROM: Sheryl Beauvais
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445-4268

DATE: September 10, 2007

SUBJECT: RESPONSE TO AIR RESOURCES BOARD COMMENTS ON ENDOSULFAN RISK CHARACTERIZATION DOCUMENT

The Department of Pesticide Regulation's (DPR's) revised final draft Risk Characterization Document (RCD) for endosulfan, dated July 2007, was posted on DPR's website for public comment. The Air Resources Board (ARB) sent two comments, dated August 21, 2007, on the RCD, including the executive summary and the draft exposure assessment document (EAD). Both comments corrected erroneous statements, and are summarized below. The comments and additional reviews are appreciated. Changes have been communicated to the risk assessor for incorporation into the RCD.

1) Distances from application to samplers: The distances of samplers from orchard edges during application site monitoring were variously reported in the RCD text and the executive summary. The range of distances is 6-16 m. This has been corrected.

2) Exposure assessment: In the Exposure Appraisal section of the EAD, it was stated that, "Airborne concentrations of active ingredients generally decrease as distance from the application site decreases..." It has been corrected to state that concentrations decrease as distance increases.

DATE: October 22, 2007

TO: Gary T. Patterson, Ph.D., Chief
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FROM: Marilyn Silva, Ph.D., D.A.B.T., Toxicologist
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VIA: Joyce Gee, PhD., Senior Toxicologist,
Medical Toxicology Branch,
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SUBJECT: DPR RESPONSE TO THE CALIFORNIA COTTON GINNERS AND GROWERS ASSOCIATIONS COMMENTS ON THE PRELIMINARY REPORT – "ENDOSULFAN-RISK CHARACTERIZATION DOCUMENT"

Following below are the responses to the California Cotton Ginners and Growers Associations (CCGGA) comments on the preliminary report on the endosulfan Risk Assessment Document (RCD).

CCGGA Comment (page 2 paragraph 3):

Page 110 – 111 – Dietary Exposure: "Once again, the usage of endosulfan plays a key role here. We feel strongly that the usage of endosulfan has decreased and will continue to decrease. Accordingly, any risk assessment on dietary exposure should reflect the most current usage data."

DPR RESPONSE: A review of the tolerance, usage, residue, consumption, prior Margins of Exposure (MOEs), and Continuing Survey of Food Intakes by Individuals (CSFII) information indicates that an update of the endosulfan dietary exposure assessment is not necessary. The CSFII is an annual survey that reflects the current consumption pattern and has a greater focus on consumption data for vulnerable population subgroups (e.g. infants and children). While the average consumption rates increased for some commodity/ population sub-group combinations in the 1994-98 CSFII survey versus the 1989-92 CSFII, this would likely be mitigated by existing tolerance cancellations and proposed revocations, and reduced annual maximum applications. In addition, if the DPR acute dietary exposure analysis were updated, there would

be a change to Monte Carlo distributional iterations for many commodities where acute percent crop treated (%CT) estimates could be incorporated. Using updated residue, consumption, and the USEPA endosulfan Risk Estimation Document (RED) tolerance and use information, the DPR acute dietary exposure assessment would likely be lower. This conclusion would hold even though MOEs at the 99.9th percent level of acute exposure would be reported instead of the 95th percent level of exposure MOEs used in the existing point estimate DPR dietary analysis. This conclusion is supported by the acceptable acute MOEs reported in the 2002 USEPA draft endosulfan RED (USEPA, 2002).

A new DPR acute dietary exposure analysis would: 1) update the residue data of the remaining commodities with tolerances, 2) delete the 9 commodity tolerances from the dietary residue file that have been canceled by the registrants since 1998, 3) delete the USEPA draft endosulfan RED proposed tolerance revocations (succulent bean and pea, grape, pecan, and spinach), 4) use more realistic residue data (e.g. exclude melon rinds), 5) use processed food forms when available instead of the raw forms as surrogates (e.g. apple juice instead of raw apples representing apple juice) for processed forms, 6) use Monte Carlo distributional iterations to replace point estimates whenever appropriate, and 7) incorporate acute %CT data into any distributional analysis (Monte Carlo). The updated DPR acute dietary exposure analysis would be very similar to the acute dietary analysis referenced in the 2002 USEPA endosulfan RED (USEPA, 2002)

The existing DPR 1998 endosulfan dietary exposure assessment reports MOEs greater than 100 for both the acute and chronic scenarios (Carr, 1998). Acute MOEs at the 95th percent level of exposure ranged from 212 for children 1-6 years to 513 for males 13-19 years population subgroups. The chronic MOEs ranged from 1,407 for children 1-6 years to 7,421 for nursing infants at less than or equal to 1 year old.

The USEPA 2002 endosulfan draft RED concluded that infants and children acute dietary exposure risk is mitigated by their tolerance revocations and proposed label changes and therefore, no longer a concern. The USEPA endosulfan RED concluded that adult acute and chronic dietary exposures are also not a concern. The conclusions resulting from an updated DPR dietary exposure assessment would likely be similar to those reported in the USEPA 2002 endosulfan RED. Therefore, a complete revision of the DPR 1998 dietary exposure assessment would appear unnecessary and the 2006 dietary exposure addendum suffices when combined with the prior 1998 DPR dietary exposure assessment.

For further discussion please see Appendices A, B and C of the Risk Assessment Document.

Dietary Exposure and the FQPA Safety Factor:

With regard to the effect of dietary exposure and the FQPA Safety Factor, the current dietary exposures used in the RCD provide sufficiently high MOEs to protect infants and children exposed to endosulfan in diet, as detailed below.

Acute and Chronic Oral RfDs:

DPR has revised the entire FQPA section, providing evidence for retaining an FQPA Factor of 1. There is a discussion of issues related to the FQPA in E. ISSUES RELATED TO THE FQPA. Although endosulfan has effects in the male reproductive system as have been described in this document, doses that would protect for neurotoxicity would also protect for endocrine disruption (observed only at higher doses). The USEPA is currently evaluating their position on endosulfan as an endocrine disruptor and on the use of the FQPA Safety Factor (SF). DPR considers that it is not necessary to use an additional FQPA SF for endosulfan based on recently submitted data and re-evaluation of previously submitted data and more recent reports in the open literature.

DPR agrees with the use of a dietary FQPA Safety Factor of 1 for endosulfan to sufficiently protect infants and children at this time.

Department of Pesticide Regulation

Mary-Ann Warmerdam
Director

M E M O R A N D U M

Arnold Schwarzenegger
Governor

TO: Joseph P. Frank
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Worker Health and Safety Branch

FROM: Sheryl Beauvais
Staff Toxicologist (Specialist)
445-4268

DATE: November 5, 2007

SUBJECT: RESPONSE TO CALIFORNIA COTTON GINNERS AND GROWERS ASSOCIATIONS (CCGGA) COMMENTS ON ENDOSULFAN RISK CHARACTERIZATION DOCUMENT

The California Department of Pesticide Regulation's (DPR's) revised final draft Risk Characterization Document (RCD) for endosulfan was posted on DPR's website in July 2007 for public comment. The California Cotton Ginners and Growers Associations (CCGGA) sent comments dated August 13, 2007. Worker Health and Safety Branch responses to comments pertaining to the Exposure Assessment Document (EAD) are summarized below. The Medical Toxicology Branch will respond separately to comments from CCGGA that are pertinent to the hazard identification and risk assessment, and the Environmental Monitoring Branch will respond to comments regarding the Environmental Fate Document.

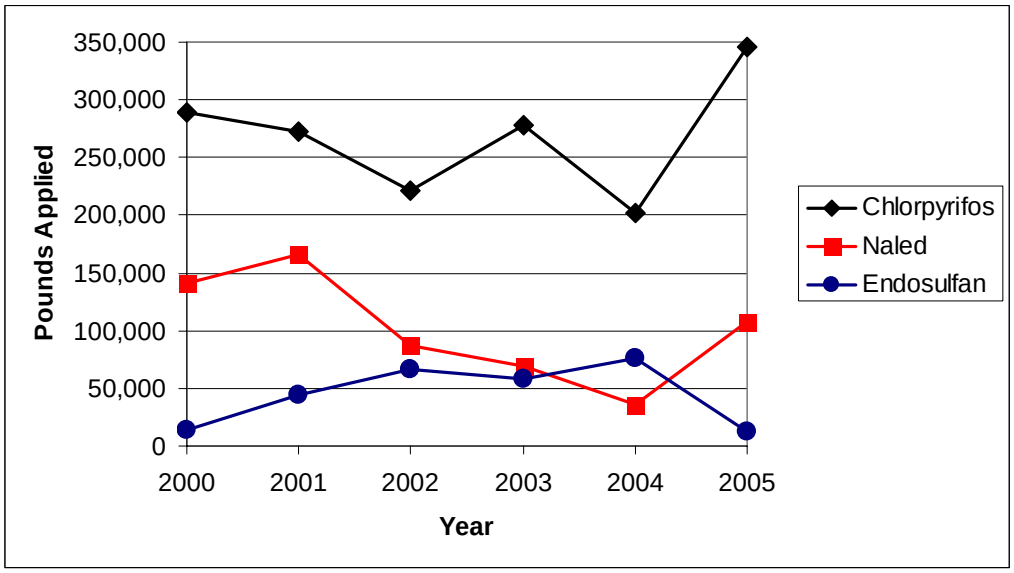
I. Endosulfan Risk Characterization Document

A. Page 21: Usage: Decline in Cotton Acreage: This comment requested that decreasing cotton acreage, and decreasing endosulfan use on cotton, be reflected in the exposure estimates. The EAD is in revision and will include 2005 pesticide use data. These data suggest that endosulfan use decreased between 2004 and 2005; the decline was mostly due to decreased use on cotton, correlating to fewer acres of cotton having been planted (DPR, 2006b). As noted by CCGGA, in 2005 cotton was not the top crop receiving endosulfan applications. In 2005, cotton ranked below tomatoes, lettuce, and alfalfa in pounds of endosulfan applied.

However, pesticide use on individual crops can fluctuate from year to year, and there is no mechanism in place to prevent endosulfan use from increasing again in the future on this or any other crop. Figure 1 illustrates this point for endosulfan and two other insecticides used on cotton, chlorpyrifos and naled. Use of both organophosphates on cotton increased sharply in 2005, in spite of the decrease in acres planted (DPR, 2006c). To minimize the effects of annual fluctuations, when determining use patterns for seasonal and annual exposure estimates DPR practice is to average use over a recent 5-year interval, rather than to focus on use in a single year. Use patterns for endosulfan on

cotton were nearly identical between the intervals 2000-2004 and 2001-2005; peak use occurred in August through October in both intervals.

Figure 1. Use of Chlorpyrifos, Naled and Endosulfan on Cotton in California [a]



[a] Data from DPR (2001, 2002, 2003, 2005, 2006a, 2006c).

B. Page 21: Usage: Alternative Pesticides: This comment stated that cotton growers are switching from endosulfan to newer products such as neonicotinoids thioamethoxam and acetamiprid, the pyridinecarboxamide flonicamid, and insect growth regulators. In the risk assessment process, DPR relies on existing data, including recent use patterns. When the risk assessment process has been completed, if DPR determines that some endosulfan uses require mitigation, then the potential impacts of alternative products on endosulfan use might be appropriately considered.

C. Page 98: Exposure Assessments: Aerial Applications: This comment disagrees with DPR's approach to aerial applicator exposure estimates. DPR assumes that some aerial applicators of endosulfan might have open cockpits, as there is no legal requirement for closed cockpits. Citing information from the California Agricultural Aircraft Association (CAAA), CCGGA states that no open cockpit aircraft are used make pesticide applications. However, CAAA membership consists of operators, pilots, and others associated with the professional aerial application industry. DPR lacks information on the proportion of all aerial applicators in California who are CAAA members and cannot assume that all applicators (e.g., grower-applicators) are members. In fact, a 2003 survey conducted by the National Agricultural Aviation Association (NAAA) received 31 responses from California; the survey responses identified one aircraft (out of 103 for

California respondents) that had an open cockpit (NAAA, 2004). It's possible that more open cockpit aircraft would be revealed in a survey with a broader response. Thus, the most recent information available about equipment used by aerial applicators shows that while open cockpits are relatively rare, they may still be used in California.

Furthermore, modern aircraft with closed cockpits can be modified by opening windows or removing doors, which would allow the pilot contact with sprays. For example, enforcement staff at DPR regional offices have observed that during hot summer days doors are often removed from helicopters, resulting in open cockpits during application. Such practices are legal in the absence of label requirements for closed cockpits during aerial applications, and under current product labels DPR must continue to include open cockpit aerial applicator scenarios in its exposure assessment.

D. Page 110 - 111: Dietary Exposure: The Medical Toxicology Branch will respond to this comment.

E. Page 129 – 131: Air – All Populations: This comment notes that endosulfan use has decreased since ambient air monitoring was conducted in 1996, and states the belief of the CCGGA that endosulfan use will continue to decrease, leading to decreased ambient air exposures. In the risk assessment process, DPR relies on existing data, including concentrations of endosulfan in air. When the risk assessment process has been completed, if DPR determines that some endosulfan uses require mitigation, then the potential impacts of declining use on future endosulfan concentrations might be appropriately considered.

F. Page 158: Re-entry Exposure Estimates: This comment notes that all reentry activities in cotton would not be anticipated to have identical exposures, and states that certain reentry activities (hand weeding and roguing) are no longer performed by growers belonging to the CCGGA.

The rationale behind assessing representative scenarios, including cotton scouting, is given on page 14 of the EAD:

> Endosulfan is registered for use on numerous crops, and many reentry activities are possible in each crop. It would be desirable to have exposure estimates for each of these crop/activity combinations (scenarios). However, little information is available for many scenarios, and several scenarios are likely to result in similar exposures. For these reasons, representative reentry exposure scenarios were selected based on available information about the extent of foliar contact for each activity, and the resulting potential for residue transfer.

DPR understands that not all reentry scenarios within a crop have identical exposure. As explained on pages 15 – 16 of the draft EAD:

> Scenarios grouped under a representative scenario are not all expected to have identical exposures; however, the representative scenario is anticipated to involve exposures similar to or greater than all scenarios covered by it. In other words, representative scenarios might overestimate exposure for other scenarios, but should not underestimate exposure. For example, cotton scouting is the representative scenario that covers all activities in alfalfa, barley, clover, oats, rye, safflower, sunflower, and wheat. Because of the height and foliar density of cotton as it matures, reentry into a treated field is likely to result in more exposure than reentry in alfalfa or most other field crops (except corn and tobacco, which are covered by another scenario). Additionally, many activities in these crops, such as irrigating or mechanical harvesting, would be anticipated to result in lower exposures per full workday than cotton scouts.

As the risk assessment is conducted on a single representative scenario for cotton, during mitigation all scenarios covered by the representative scenario would be individually assessed along with the representative scenario. In many cases, it is likely that at least some of the scenarios covered by a representative scenario will have exposure estimates substantially below that of the represented scenario. When the risk assessment process has been completed, if DPR determines that endosulfan use on cotton requires mitigation, then the extent to which individual scenarios are performed in California can be addressed.

II. Appendix E: Estimation of Exposure of Persons in California to Pesticide Products That Contain Endosulfan

A. Page 8: Pesticide Use and Sales: This comment references comments addressed in responses I.A. and I.B. above. Responses to referenced comments explain DPR's rationale for exposure estimates.

B. Page 12: Exposure Scenarios: This comment states that according to CAAA human flaggers are no longer used in California, and asks that the scenario be deleted. While DPR recognizes that the use of human flaggers is becoming increasingly rare as newer technologies are adopted, as explained above in response I.C. DPR cannot be certain of the extent to which information reported by CAAA covers all aerial applications occurring in California. Until use of human flaggers is prohibited, DPR must continue to consider this scenario.

C. Page 28: Ambient Air: This comment references the comment addressed in response I.E. above. Response I.A., I.B., and I.E. explain DPR's rationale for using existing monitoring data to estimate exposures.

D. Page 42: Aerial Applications: This comment references the comment addressed in response I.C. above. The response to the referenced comment addresses this comment as well.

E. Page 71: Reentry Exposure Assessment: This comment references the comment addressed in response I.F. above. The response to the referenced comment addresses this comment as well.

III. Endosulfan Exposure Assessment

A. Page 8: Pesticide Use and Sales: This comment states that the use of endosulfan on cotton to control the Silverleaf Whitefly has been largely replaced by two other chemicals, pyriproxyfen and buprofezin. The comment requests that use and sales data be updated to include 2005 data, and 2006 when available. The EAD is in revision and will include 2005 pesticide use data.

B. Page 14: Exposure Scenarios - Re-entry: This comment references the comment addressed in response I.F. above. The response to the referenced comment addresses this comment as well.

C. Page 29: Environmental Concentrations - Ambient Air: This comment references the comment addressed in response I.E. above. Response I.A., I.B., and I.E. explain DPR's rationale for using existing monitoring data to estimate exposures.

D. Page 72: Reentry Exposure Estimates: This comment references the comment addressed in response I.F. above. The response to the referenced comment addresses this comment as well.

E. Page 91: Appendix I: Agricultural Reentry Scenarios Table: This comment references the comment addressed in response I.F. above. The response to the referenced comment addresses this comment as well.

References

Air Resources Board (ARB). 1998. Report for the Air Monitoring of Endosulfan in Fresno County (Ambient) and in San Joaquin County (Application). Project No. C96-

034. Sacramento, CA: Engineering and Laboratory Branch, Air Resources Board, California Environmental Protection Agency.

DPR. 2001. Summary of Pesticide Use Report Data 2000: Indexed by Commodity. Report dated October 2001. Sacramento, CA: Department of Pesticide Regulation, California Environmental Protection Agency.

DPR. 2002. Summary of Pesticide Use Report Data 2001: Indexed by Commodity. Report dated October 2002. Sacramento, CA: Department of Pesticide Regulation, California Environmental Protection Agency.

DPR. 2003. Summary of Pesticide Use Report Data 2002: Indexed by Commodity. Report dated October 2003. Sacramento, CA: Department of Pesticide Regulation, California Environmental Protection Agency.

DPR. 2005. Summary of Pesticide Use Report Data 2003: Indexed by Commodity. Report dated January 2005. Sacramento, CA: Department of Pesticide Regulation, California Environmental Protection Agency.

DPR. 2006a. Summary of Pesticide Use Report Data 2004: Indexed by Commodity. Report dated January 2006. Sacramento, CA: Department of Pesticide Regulation, California Environmental Protection Agency.

DPR. 2006b. Summary of Pesticide Use Report Data 2005: Indexed by Chemical. Report dated November 2006. Sacramento, CA: Department of Pesticide Regulation, California Environmental Protection Agency.

DPR. 2006c. Summary of Pesticide Use Report Data 2005: Indexed by Commodity. Report dated November 2006. Sacramento, CA: Department of Pesticide Regulation, California Environmental Protection Agency.

NAAA. 2004. Pesticide Use Survey Report for Agricultural Aviation: A Study Conducted by the National Agricultural Aviation Association (NAAA). Unpublished report dated May 2004.

U.S. EPA. 2002. Reregistration Eligibility Decision for Endosulfan. Case 0014. Washington, DC: Office of Prevention, Pesticides and Toxic Substances, U.S. Environmental Protection Agency.

TO: Pam Wofford
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Environmental Monitoring Branch

FROM: Shifang Fan
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324-4096

DATE: November 16, 2007

SUBJECT: RESPONSE TO CALIFORNIA COTTON GINNERS AND GROWERS ASSOCIATIONS (CCGGA) COMMENTS ON ENDOSULFAN RISK CHARACTERIZATION DOCUMENT, VOLUME III

The California Department of Pesticide Regulation's (DPR's) draft Risk Characterization Document (RCD) for endosulfan was posted on DPR's website in July 2007 for public comment. The California Cotton Ginners and Growers Associations (CCGGA) sent comments dated August 13, 2007. Environmental Branch's responses to comments pertaining to the Environmental Fate are summarized below.

Endosulfan Environmental Fate -

A. Page 10, Use Profile in California, "As stated previously, endosulfan usage is on the decrease, especially on cotton. Th environmental fate determination must be revised to reflect this".

Response: The following text and maps were added to the revised document: A side-by-side comparison of the use maps for 1997 and 2005 show decreased endofulfan use in 2005, mainly due to reduction of cotton crop in the San Joaquin Valley (Figure 4). Endosulfan use on cotton decreased 87% in 2005 vs 1997 in the top six counties.

B. Page 18-28, References to Studies on Endosulfan Applied to Cotton in Australia, "The document continually refers to measurements taken in Australia, where endosulfan is a much more prevalent insecticide. Any measurements taken in Australia will not reflect use patterns nor total use amounts in 2007".

Response: The information and discussion were references in general, not particularly to reflect use patterns in California.

C. Page 30, Ambient Air Monitoring, "The document provides additional insight to the ambient air monitoring performed by ARB in 1996. Here the document indicates that the monitoring sites were only 50 to 100 yards away. Again, this

monitoring was conducted during a time period when endosulfan was much more prevalent and just a short distance from a cotton field. This would not be reflective of an average person exposure in the San Joaquin Valley, especially now. The monitoring data is outdated and overstates the true exposure for valley residents".

Response: The selected monitoring locations were populated areas, such as schools, and surrounded on all directions by farmland. Ccotton was planted approximately 50 to 100 yards from two monitoring locations and ¾ to 2 miles from the other two locations. During monitoring period, there might or might not have been endosulfan use in the surrounding farmland. Endosulfan was detected at all locations regardless how far from farmland. The highest concentration was at a location ¾ to 1 mile from the closest farmland. ARB's ambient monitoring results were used in this document since it was conducted during the highest use year representing the worst scenario of exposure.

DATE: October 22, 2007

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VIA: Joyce Gee, PhD., Senior Toxicologist,
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SUBJECT: MAKHTESHIM AGAN OF NORTH AMERICA, INC. (MANA) RESPONSE TO CDPR'S PRELIMINARY LISTING OF ENDOSULFAN AS A TOXIC AIR CONTAMINANT

Following below are the responses to the MANA recommendations.

MANA's Comment, Page 5: III. REBUTTAL TO USING A 1000-FOLD MARGIN OF EXPOSURE FOR THE BASIS OF LISTING COMPOUNDS AS A TOXIC AIR CONTAMINANTS.

CDPR notes that the applicable legislation mandating TAC review states that the threshold for listing compounds is ten-fold below the level that the Director judges is safe; that is, ten-fold below a level that is 100-fold below the no adverse effect level (NOAEL) in an appropriate toxicological study (Silva, 2007). This 'safety factor upon safety factor" results in a threshold that is 1000 times below the no effect level for each compound considered. CDPR acknowledges that 100-fold (Dourson et al., 2002) is normally adequate but children require 1000-fold safety (Silva et al., 2006). There is insufficient toxicological basis for the additional 10-fold safety factor. Legislative mandate is, in effect, a political judgment where judgments should be left to science.

DPR Response: DPR complies with the California Code of Regulations (Title 3. Food and Agriculture; Division 6. Pesticides and Pest Control Operations; Chapter 4. Environmental

Protection; Subchapter 2. Air; Article 1. Toxic Air Contaminants; 6860. Toxic Air Contaminants List).

MANA's Comment, Page 6: CDPR notes that there are three operable NOAELs for risk assessments: acute effects = 0.7 mg/kg/day; subchronic effects = 0.194 mg/kg/day; and chronic effects = 0.57 mg/kg/day. While CDPR choose [sic] to use the subchronic NOAEL for calculaltion of endosulfan MOEs, use of the acute or chronic NOAELs would increase the resultant MOEs in an arithmetic manner.

DPR Response: DPR has elected to use the NOELs available for inhalation exposure since an acceptable study has been performed. The rationale for use of the inhalation NOEL has been further explained in the report.

An acute inhalation (LC_{50}) study was performed (Hollander and Weigand, 1983), however a NOEL was not achieved (LOEL = 0.567 mg/kg). Therefore, an acceptable subchronic rat inhalation study (based on a subchronic rangefinding study with a LOEL of 0.44 mg/kg reported within Hollander et al., 1984) with a NOEL of 0.0010 mg/L (0.194 mg/kg/day; LOEL = 0.387 mg/kg/day) was used to calculate the potential for acute single-day inhalation exposure to workers, and for exposure to endosulfan in ambient air or to bystanders (Hollander et al., 1984). The rationale for the use of the subchronic inhalation study for the Acute NOEL is that LOELs from all three studies were similar (0.567, 0.44 and 0.387 mg/kg/day), more animals treated in the subchronic (15/sex/dose subchronic versus 5/sex/dose in the acute), and the subchronic study used a 29 day recovery with 5 per sex per dose (acute 14d observation). The NOEL of 0.194 mg/kg/day is a reasonable selection based on the LOELs from the 3 studies. It is also a conservative estimate for an acute NOEL, since acute NOELs are usually higher than subchronic or chronic NOELs. It is also noted that all three studies were performed at the same laboratory and in the same timeframe (12/7/83—Acute; 8/15/83--Subchronics).

MANA Comment, page 6: V. CONCLUSION
Based on the questionable monitoring data (unreliable, questionable analytical standards, not representative, unrealistic usage data), and in view of the additional 10-fold safety factor (total of 1000-fold), which stands in opposition to the mandates of the California TAC legislation, there should be no risk or harm to the public by airborne endosulfan exposure. Therefore, endosulfan should not be listed as a toxic air contaminant.

DPR Response: DPR has used the best data available to obtain exposure and has selected the most reasonable NOELs for inhalation. Since there are several MOEs that fall below 1000, DPR presents data to the Scientific Review Panel for consideration that endosulfan be listed as a TAC.

TO: Joseph P. Frank
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FROM: Sheryl Beauvais
Staff Toxicologist (Specialist)
445-4268

DATE: November 14, 2007

SUBJECT: RESPONSE TO MAKHTESHIM AGAN OF NORTH AMERICA, INC. COMMENTS ON ENDOSULFAN RISK CHARACTERIZATION DOCUMENT

The California Department of Pesticide Regulation's (DPR's) revised final draft Risk Characterization Document (RCD) for endosulfan was posted on DPR's website in July 2007 for public comment. Makhteshim Agan of North America, Inc. (MANA) sent comments via email on August 23, 2007. No changes were made to the Exposure Assessment Document (EAD) in response to these comments. Worker Health and Safety Branch responses to comments pertaining to the EAD are summarized below. The Medical Toxicology Branch will respond separately to comments from MANA that are pertinent to the hazard identification and risk assessment.

I. Rebuttal to Assumptions for Agricultural Spraying in Sampling Area

This comment asks that exposure estimates reflect mitigation measures proposed in the Reregistration Eligibility Decision released in 2002 by the U.S. Environmental Protection Agency (U.S. EPA, 2002). However, not all current product labels reflect mitigation measures proposed by U.S. EPA (2002). The EAD estimates exposures to the active ingredient (AI), based on uses and directions on all active product labels approved by DPR for that AI. If DPR determines that some endosulfan uses require mitigation, then this will be done for each product, based on individual product labels.

Additionally, this comment requested that decreasing endosulfan use reported in recent years be reflected in the exposure estimates. The EAD is in revision and will include 2005 pesticide use data from DPR's Pesticide Use Report. These data suggest that endosulfan use decreased between 2004 and 2005; the decline was mostly due to decreased use on cotton, correlating to fewer acres of cotton having been planted (DPR, 2006). Pesticide use on individual crops can fluctuate from year to year, and there is no mechanism in place to prevent endosulfan use from increasing again. For this reason, DPR has not adjusted exposure estimates for recent use changes.

Finally, this comment asserts that because relatively few acres of crops receiving airblast applications were treated with endosulfan in 2005, air monitoring of an airblast application is not representative of endosulfan use in California. However, decreasing endosulfan use on crops receiving airblast applications does not lessen the usefulness of the airblast application monitoring study conducted by the California Air Resources Board (ARB, 1998).

Bystander exposure scenarios make use of application site monitoring data to estimate the exposure of any individual, located near a treated area during or following a pesticide application, who is not involved in the application. Bystanders can be adjacent to any type of application allowed for endosulfan, including airblast. As long as airblast is an allowed application method, use of the airblast application site air monitoring data is appropriate.

II. Rebuttal to Using 1996/1997 Sampling Data as a Basis for Determining Risk to Persons Exposed to Ambient Air and Bystanders

This comment asserts that air monitoring data from ARB (1998) should not be used to estimate exposure, because of unacceptable quality assurance (QA) and because of insufficient sampling sites and sampling intervals for ambient air monitoring.

Spiked samples for ambient air monitoring had low α-endosulfan recoveries, with mean field spike recovery of 44%, and spiked samples for application site monitoring had low β-endosulfan recoveries, with mean field spike recovery of 60%. These recoveries are low, but not necessarily unacceptable. In fact, the good laboratory practice discussed by U.S. EPA (1996) and Jiang (2005), which were cited in this comment, set a recovery range of 70 – 120% as part of the criteria to be met during method validation. DPR and U.S. EPA will not generally accept analytical methods that can't meet these criteria, but will accept well-conducted field studies where spike recoveries are outside that range. Method validation recoveries of both α-endosulfan and β-endosulfan were within the range of 70 – 120%; Table 1 summarizes the method validation recoveries reported by ARB (1998).

The ambient air and application site monitoring studies by ARB were well-conducted studies. These studies provide the best available data for endosulfan concentrations in air, and DPR will continue to rely on data from ARB (1998) to estimate bystander and ambient air exposures to endosulfan.

A total of four ambient air sample sites were monitored in 1996. The sites were selected to be in areas where past endosulfan use was high, in cotton and grape growing areas in Fresno County. Additionally, sampling occurred during a high-use time. The purpose of

ambient air sampling is to assess endosulfan concentrations in air in public locations in high-use areas during high-use times. In response to comments from the Scientific Review Panel on Toxic Air Contaminants, DPR has determined that the most health protective estimates for airborne exposures to the public are based on application site monitoring. Accordingly, in its revised risk assessment DPR based all exposure estimates on concentrations from application site monitoring.

Table 1. Endosulfan Recoveries During Method Validation [a]

Procedure	Percent Recovery [b] α-Endosulfan	β-Endosulfan
Collection and Extraction Efficiency [c]		
Samples spiked at 0.050 µg	101 ± 1	81 ± 3
Samples spiked at 0.150 µg	90 ± 1	71 ± 1
Storage Stability [d]		
Samples stored for 0 days	95 ± 2	84 ± 5
Samples stored for 2 days	102 ± 1	81 ± 1
Samples stored for 7 days	105 ± 2	87 ± 3
Samples stored for 20 days	103 ± 1	89 ± 3

[a] Data from the California Air Resources Board (ARB, 1998); method validation procedures are described in ARB (1999). All recoveries were within the ARB (1999) criteria range (70 – 130%).
[b] Mean ± standard deviation of three samples.
[c] Triplicate samples spiked and placed in a sampler set at a flow rate of 2 liters per minute for 24 hours before extraction and analysis.
[d] Triplicate samples spiked at 0.050 µg and placed in storage at 4°C for up to 20 days before extraction and analysis.

III. Rebuttal to Using a 1000-Fold Margin of Exposure for the Basis of Listing Compounds as Toxic Air Contaminants

The Medical Toxicology Branch will respond to this comment.

IV. Rebuttal to the Proposed Listing of Endosulfan as a Toxic Air Contaminants

The Medical Toxicology Branch will respond to this comment.

References

Air Resources Board (ARB). 1998. Report for the Air Monitoring of Endosulfan in Fresno County (Ambient) and in San Joaquin County (Application). Project No. C96-

034. Sacramento, CA: Engineering and Laboratory Branch, Air Resources Board, California Environmental Protection Agency.
http://www.cdpr.ca.gov/docs/empm/pubs/tac/endoslfn.htm

ARB. 1999. Quality Assurance Plan for Pesticide Monitoring. Appendix A in: Report for the Application and Ambient Air Monitoring for Benomyl. Sacramento, CA: Engineering and Laboratory Branch, Air Resources Board, California Environmental Protection Agency. Appendix A in:
http://www.cdpr.ca.gov/docs/empm/pubs/tac/benarbap.pdf

DPR. 2006. Summary of Pesticide Use Report Data 2005: Indexed by Chemical. Report dated November 2006. Sacramento, CA: Department of Pesticide Regulation, California Environmental Protection Agency.

Jiang, W. 2005. Good laboratory practice in analytical laboratory. The Journal of American Science 1:93-94.

U.S. EPA. 1996. Residue Chemistry Test Guidelines: Residue Analytical Method (OPPTS 860.1340). EPA 712–C–96–174 August 1996.

U.S. EPA. 2002. Reregistration Eligibility Decision for Endosulfan. Case 0014. Washington, DC: Office of Prevention, Pesticides and Toxic Substances, U.S. Environmental Protection Agency.

DATE: October 22, 2007

TO: Gary T. Patterson, Ph.D., Chief
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FROM: Marilyn Silva, Ph.D., D.A.B.T., Toxicologist
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California Environmental Protection Agency

VIA: Joyce Gee, PhD., Senior Toxicologist,
Medical Toxicology Branch,
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California Environmental Protection Agency

SUBJECT: DPR RESPONSE TO THE LATINO ISSUES FORUM: A PUBLIC POLICY & ADVOCACY INSTITUTE COMMENTS IN RESPONSE TO THE RISK CHARACTERIZATION DOCUMENT FOR ENDOSULFAN

Following below are the responses to the Latino Issues Forum recommendations.

Latino Issues Forum (page 2 paragraph 2):

Reference was made to the recent study entitled "Maternal residence near agricultural pesticide applications and autism spectrum disorders among children in the California Central Valley.," (Roberts et al., 2007; Environmental Health Perspectives, 115(10):1482-1489). The Latino Issues Forum related "This study was extremely alarming to us because it reiterates the community testimony we have heard over the last several years. Community members living [in] agricultural San Joaquin Valley communities like Huron, where endosulfan is heavily used, have stated specifically, on numerous occasions, that they have seen higher rates of Autism in children in recent years, and that they believe it is related to the toxic pesticides drifting off the fields. Many of our constituents live in communities completely surrounded by fields where Endosulfan [is sprayed?] and reside in homes literally across the street from fields where Endosulfan is regularly sprayed."

DPR Response: The use of endosulfan has been declining throughout the time the study was performed but Autism has been on the rise nation-wide. DPR has added a summary of the Roberts et al (2007) study, our conclusions and a summary of the comments from other reviewers to the risk assessment.

Endosulfan exposure in ambient air near agricultural applications to pregnant women was proposed to induce neurotoxicity in fetuses when exposure occurred during gestation weeks 1 through 8 (period of central nervous embryogenesis) (Roberts et al., 2007). Exposure was proposed to result in an increased incidence in autism spectrum disorder (ASD). This study was very preliminary and contained numerous deficiencies acknowledged by the authors. DPR made mention of the Roberts study in the RCD. However, due to deficiencies, it cannot be used for regulatory purposes.

Department of Pesticide Regulation

Mary-Ann Warmerdam
Director

M E M O R A N D U M

Arnold Schwarzenegger
Governor

TO: Joseph P. Frank
Senior Toxicologist
Worker Health and Safety Branch

FROM: Sheryl Beauvais
Staff Toxicologist (Specialist)
445-4268

DATE: November 14, 2007

SUBJECT: RESPONSE TO LATINO ISSUES FORUM COMMENTS ON ENDOSULFAN RISK CHARACTERIZATION DOCUMENT

The Department of Pesticide Regulation's (DPR's) revised final draft Risk Characterization Document (RCD) for endosulfan was posted on DPR's website in July 2007 for public comment. The Latino Issues Forum sent comments dated August 24, 2007, in support of listing endosulfan as a Toxic Air Contaminant (TAC), and further urge DPR to require that endosulfan use be discontinued. Statements from the RCD were cited in support of these positions. None of the comments suggest that changes in the Exposure Assessment Document (EAD) are needed, although references were made to levels of exposure to endosulfan.

Since the EAD was released for public comment, it has been updated to include 2005 pesticide use data. These data suggest that endosulfan use decreased between 2004 and 2005; the decline was mostly due to decreased use on cotton, correlating to fewer acres of cotton having been planted (DPR, 2006). Pesticide use on individual crops can fluctuate from year to year, and there is no mechanism in place to prevent endosulfan use from increasing again. For this reason, DPR has not adjusted exposure estimates for recent use changes.

Once the draft RCD has been finalized, the risk assessment process will be complete for endosulfan. DPR will then determine appropriate risk management steps. Listing as a TAC is one of several options available to address risks associated with endosulfan uses. A brief summary of DPR's risk management process is given in DPR (2001).

Reference

DPR. 2001. Regulating Pesticides: The California Story. A Guide to Pesticide Regulation in California. Chapter 5: Assessing Pesticide Risks. Sacramento, CA: Department of Pesticide Regulation, California Environmental Protection Agency.

DPR. 2006. Summary of Pesticide Use Report Data 2005: Indexed by Chemical. Report dated November 2006. Sacramento, CA: Department of Pesticide Regulation, California Environmental Protection Agency.

DATE: October 22, 2007

TO: Gary T. Patterson, Ph.D., Chief
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VIA: Joyce Gee, PhD., Senior Toxicologist,
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SUBJECT: DPR RESPONSE TO PESTICIDE ACTION NETWORK (PAN) COMMENTS ON THE RISK CHARACTERIZATION DOCUMENT DEVELOPED FOR THE EVALUATION OF ENDOSULFAN AS A POTENTIAL TOXIC AIR CONTAMINANT

The DPR response to the Pesticide Action Network comments on endosulfan (August 24, 2007).

PAN Comment (page 4 paragraph 1):

Reference was made to the recent study entitled "Maternal residence near agricultural pesticide applications and autism spectrum disorders among children in the California Central Valley.," (Roberts et al., 2007; Environmental Health Perspectives, 115(10):1482-1489).

DPR Response: The use of endosulfan has been declining since the time the study was performed (1996-1998) but Autism has been on the rise nation-wide. In our document, we added a brief summary of the study and our conclusions along with the general consensus from other reviewers and the media as to the bottom line.

Endosulfan exposure in ambient air near agricultural applications to pregnant women was proposed to induce neurotoxicity in fetuses when exposure occurred during gestation weeks 1 through 8 (period of central nervous embryogenesis) (Roberts et al., 2007). Exposure was proposed to result in an increased incidence in autism spectrum disorder (ASD). Conclusions to this study that the association between endosulfan and pesticide applications during gestation and autism in children needs further study. This study was very preliminary

and numerous defects were discussed in a report by Edreich and Morimoto (2007). This study was included in this report but cannot be used for regulatory purposes.

Please also see Environmental Health Perspectives "Autism and Agricultural Pesticides: Integrating Data to Track Trends," EHP, 115(10):A504. The reviewer concludes that "Although the association between organochlorine exposure and ASDs points to a connection between the two, it does not indicate causality and does not consider other factors that may be involved. For the residences nearest to the organochlorine application sites (where the ASD association was the strongest), data around exposures came from only 8 cases and 105 controls." Numerous factors, such as diet, were not examined. The critical review by Erdreich and Morimoto (2007) is highly analytical. Erdreich, L., Morimoto, L., 2007. Endosulfan critical review of epidemiological study "Maternal residence near agricultural pesticide applications and autism sprectum disorders among children in the California Central Valley." Makhteshim-Agan of North America Inc., Raleigh, NC 27609. Report ID: AOTO 0807 LEO1.

TO: Joseph P. Frank
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FROM: Sheryl Beauvais
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DATE: November 13, 2007

SUBJECT: RESPONSE TO COMMENTS ON ENDOSULFAN RISK CHARACTERIZATION DOCUMENT FROM THE PESTICIDE ACTION NETWORK AND CO-COMMENTERS.

The California Department of Pesticide Regulation's (DPR's) revised final draft Risk Characterization Document (RCD) for endosulfan was posted on DPR's website in July 2007 for public comment. The Pesticide Action Network (PAN) sent comments dated August 24, 2007. Comments were co-submitted by El Comité para el Bienestar de Earlimart, the Center on Race, Poverty and the Environment, the Latino Issues Forum, Neighbors at Risk, and Fresno Metro Ministry. Worker Health and Safety Branch responses to comments pertaining to the Exposure Assessment Document (EAD) are summarized below. The Medical Toxicology Branch will respond separately to comments from PAN that are pertinent to the hazard identification and risk assessment, and the Environmental Monitoring Branch will respond to comments regarding the Environmental Fate Document.

1. We support DPR's use of inhalation toxicology studies to estimate inhalation NOAELs.

The Medical Toxicology Branch will respond to this comment.

2. PAN air monitoring data taken near endosulfan application sites demonstrates inhalation exposure to be above levels of concern.

This comment included a summary of data from PAN monitoring conducted near an elementary school in Florida in 2006 (PAN, 2007). DPR appreciates having these data brought to our attention. Data reported by PAN (2007) support the health-protective nature of concentrations used to estimate bystander exposure.

Total endosulfan concentrations reported by PAN (2007) were somewhat higher than those reported in California during the 1996 ambient air monitoring study conducted by the Air Resources Board (ARB, 1998). The highest total concentration reported by PAN was 0.626 $\mu g/m^3$, while the highest concentrations reported by ARB for α- and β-

endosulfan were 0.318 μg/m^3 and 0.031 μg/m^3, respectively. Also, the mean total endosulfan concentration reported by PAN was 0.278 μg/m^3, while the mean total reported by ARB at Site SJ (the site with the highest concentrations) was 0.062 μg/m^3.

However, the highest endosulfan concentrations reported by PAN (2007) might have been affected by applications that were observed on December 6 and 13. Although these applications correlated with the highest endosulfan concentrations measured by PAN (2007), the identities of pesticides being applied were not confirmed.

In response to comments from the Scientific Review Panel on Toxic Air Contaminants, DPR has determined that the most health protective estimates for airborne exposures to the public are based on application site monitoring. Exposures to endosulfan in ambient air are anticipated to be equal to or less than bystander exposures to endosulfan, as the highest pesticide concentrations in air occur adjacent to an application (MacCollom *et al.*, 1968; Siebers *et al.*, 2003). Bystander exposure estimates are thus health-protective estimates for ambient air exposures, and separate ambient air estimates are no longer provided for endosulfan. The 24-hour time-weighted average (TWA) for the east monitoring station (24-hour TWA = 1.63 μg/m^3) was used to estimate short-term exposure; this concentration was further adjusted for the ratio between the maximum application rate allowed on apples (2.5 lbs AI/acre) and the application rate used in the study (1.5 lbs AI/acre), to give an adjusted concentration of 2.72 μg/m^3. Seasonal and annual exposure estimates were based on the 3-day TWA of 0.952 μg/m^3. Both of the concentrations used by DPR to estimate exposure are greater than concentrations reported by PAN (2007).

3. Endosulfan exposure has been linked to Autism Spectrum Disorders.

The Medical Toxicology Branch will respond to this comment.

4. Chemical structures of endosulfan isomers are incorrect.

The Medical Toxicology Branch will respond to this comment.

References

Air Resources Board (ARB). 1998. Report for the Air Monitoring of Endosulfan in Fresno County (Ambient) and in San Joaquin County (Application). Project No. C96-034. Sacramento, CA: Engineering and Laboratory Branch, Air Resources Board, California Environmental Protection Agency.

MacCollom, G.B., Johnston, D.B. and Parker, B.L. 1968. Determination and measurement of dust particles in atmospheres adjacent to orchards. Bulletin of Environmental Contamination and Toxicology 3:368-374.

Pesticide Action Network (PAN). 2007. Air Monitoring in Hastings, Florida, December 6–14, 2006: Technical Report. Report dated April 2007. San Francisco, CA: Pesticide Action Network North America.

Siebers, J., Binner, R. and Wittich, K.P. 2003. Investigation on downwind short-range transport of pesticides after application in agricultural crops. Chemosphere 51:397-407.

DATE: October 22, 2007

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SUBJECT: DPR RESPONSE TO WESTERN GROWERS' COMMENTS ON CDPR'S "ENDOSULFAN--RISK CHARACTERIZATION DOCUMENT"

Following below are the responses to the Western Growers recommendations.

Western Growers Comment (page 3 paragraph 2):

Acute and Chronic Oral RfDs:

DPR has revised the entire FQPA section, providing evidence for retaining an FQPA Factor of 1. There is a discussion of issues related to the FQPA in E. ISSUES RELATED TO THE FQPA. Although endosulfan has effects in the male reproductive system as has been described in this document, doses that would protect for neurotoxicity would also protect for endocrine disruption (observed only at higher doses). The USEPA is currently evaluating their position on endosulfan as an endocrine disruptor and on the use of the FQPA Safety Factor (SF). DPR considers that it is not necessary to use an additional FQPA SF for endosulfan based on recently submitted data and re-evaluation of previously submitted data and more recent reports in the open literature.

DPR agrees with the use of a dietary FQPA Safety Factor of 1 for endosulfan to sufficiently protect infants and children at this time.